Best practice in the management of behavioural and psychological symptoms of dementia

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Abstract: Behavioural and psychological symptoms of dementia (BPSD) occur in most patients with dementia. They cause great suffering in patients and caregivers, sometimes more so than the cognitive and functional decline inherent to dementia. The clinical features of BPSD include a wide variety of affective, psychotic and behavioural symptoms and signs. The causes and risk factors for BPSD are multiple and include biological, psychological and environmental variables. Frequently, their combination, rather than any specific factor, explains the occurrence of BPSD in an individual patient. Thus, a sound etiopathogenetic investigation including the patient and the family or care team is essential. The aim is to develop an individualized treatment plan using a therapeutic decision tree modified by the individual and environmental risk profile. Still, treatment may be difficult and challenging. Clinical empiricism often steps in where evidence from controlled studies is lacking. Psychosocial treatment approaches are pivotal for successful treatment of BPSD. Often a combination of different non-pharmacological approaches precedes drug treatment (most of which is off-label). Regular assessments of the treatment plan and any prescriptions must be carried out to detect signs of relapse and to stop any medicines that may have become inappropriate. Even with optimal management, BPSD will not disappear completely in some cases and will remain challenging for all involved parties. This article is a narrative review based closely on the interprofessional Swiss recommendations for the treatment of BPSD. To establish the recommendations, a thorough research of the literature has been carried out. Evidence-based data were provided through searches of Medline, Embase, ISI and Cochrane-Database research. Evidence categories of the World Federation of Biological Societies were used. Additionally, the clinical experience of Swiss medical experts was considered.

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Best practice in the management of behavioural and psychological symptoms of dementia

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Abstract: Behavioural and psychological symptoms of dementia (BPSD) occur in most patients with dementia. They cause great suffering in patients and caregivers, sometimes more so than the cognitive and functional decline inherent to dementia. The clinical features of BPSD include a wide variety of affective, psychotic and behavioural symptoms and signs. The causes and risk factors for BPSD are multiple and include biological, psychological and environmental variables. Frequently, their combination, rather than any specific factor, explains the occurrence of BPSD in an individual patient. Thus, a sound etiopathogenetic investigation including the patient and the family or care team is essential. The aim is to develop an individualized treatment plan using a therapeutic decision tree modified by the individual and environmental risk profile. Still, treatment may be difficult and challenging. Clinical empiricism often steps in where evidence from controlled studies is lacking. Psychosocial treatment approaches are pivotal for successful treatment of BPSD. Often a combination of different non-pharmacological approaches precedes drug treatment (most of which is off-label). Regular assessments of the treatment plan and any prescriptions must be carried out to detect signs of relapse and to stop any medicines that may have become inappropriate. Even with optimal management, BPSD will not disappear completely in some cases and will remain challenging for all involved parties. This article is a narrative review based closely on the interprofessional Swiss recommendations for the treatment of BPSD. To establish the recommendations, a thorough research of the literature has been carried out. Evidence-based data were provided through searches of Medline, Embase, ISI and Cochrane-Database research. Evidence categories of the World Federation of Biological Societies were used. Additionally, the clinical experience of Swiss medical experts was considered.

Keywords: attachment, BPSD, environmental factors, etiopathogenetic, individualized treatment, personality

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Introduction

The term behavioural and psychological symptoms of dementia (BPSD; also termed neuropsychiatric symptoms) describes the heterogeneous group of symptoms and signs of disturbed perception, thought content, mood or behaviour that frequently occur in patients with dementia.[1,2] Throughout the course of their dementia, the vast majority of patients will develop one or more BPSD.[1–6] BPSD can have serious consequences. They are associated with worsening cognition and progression to more severe stages of dementia.[7] BPSD also lead to individual suffering and impact the caregiver burden.[8] Furthermore, they increase the risk for secondary complications such as falls and fractures leading to emergency room admissions,[9] and ultimately institutionalization.[10,11] Finally, BPSD result in higher costs of therapy and caregiving.[12,13]

The treatment of patients with BPSD can be challenging for physicians and healthcare teams. The

etiopathogenesis of BPSD is often complex, with multiple contributing direct factors and indirect mediators. Biological factors (e.g. brain changes, comorbidities, medication) may interact with psychological (e.g. personal life history, personality) or social (support network, living arrangements) aspects. Consequently, treatment should be guided by a comprehensive etiopathogenetic assessment. Currently, there is limited evidence for symptomatic treatments and the available evidence-based options are only moderately effective. Psychosocial, that is non-pharmacological, approaches should be considered the mainstay of therapy and are complemented by psychotropic medication only if unavoidable. Ideally, the available treatment algorithms are used to devise an individualized treatment plan informed by a multifaceted understanding of the patient's situation, clinical experience and expert knowledge.

Clinical presentation of BPSD

The clinical presentations of BPSD include apathy, depression, anxiety, delusions, hallucinations, sexual or social disinhibition, sleep–wake cycle disturbances, aggression, agitation and other behaviours considered inappropriate.[14] There are several instruments to systematically assess the presence and severity of BPSD,[15] among which the Neuropsychiatric Inventory (NPI)[16] and Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD)[17] are recommended.[18] Some BPSD tend to cluster together, usually into four clusters – that is, the affective, psychotic, hyperactive and apathetic clusters.[1,19] In a population-based study, the cumulative incidence of having one or more NPI-measured BPSD from the onset of cognitive symptoms was 80%,[20] indicating that occurrence of BPSD has to be expected throughout the course of dementia. Apathy, depression, anxiety and agitation were found to be the most frequent forms of BPSD.[2,20,21] However, a recent systematic review revealed substantial variation in the reported prevalence, incidence and longitudinal course between different studies.[22] In an individual patient, the type and severity of BPSD tend to change over time, but some forms such as wandering seem to be more persistent.[22] Overall, the 'natural course' of BPSD over time is still largely unknown.

Depression

Most patients with dementia have depressive symptoms and signs at some point in time over the course of dementia (nearly 80% over the past 5 years). Some patients may present with a major depressive disorder (10–20%).[1] A history of depressive disorder is likely to increase the risk of major depressive disorder during dementia. Insomnia, changes in circadian rhythm and anxiety may accompany depressive symptoms. Abnormalities in the serotonin, dopamine or epinephrine systems, frontal atrophy, and amygdala reactivity may be some of the neurobiological underpinnings of depressive features.

Hallucinations

Another condition that should be considered is the Charles Bonnet syndrome, which is due to an eye disease. Visual hallucinations in Charles Bonnet syndrome are usually of short duration and patients are aware that they are not real; these hallucinations are often well tolerated by the patient and therefore may not need treatment other than that prompted by the underlying eye disease. In some instances, carbamazepine may be useful.[23] Auditory hallucinations must evoke an underlying psychotic state not primarily explained by dementia, and usually need treatment.

Agitation

In an inpatient clinical setting, agitation is often the most challenging BPSD since it may severely disrupt patient care. Hence, most treatment trials for BPSD have been performed for agitation. Agitation refers to an ill-defined spectrum of aberrant hyperactive motor behaviours (such as wandering, leaving home) and physically or verbally aggressive behaviours such as rejection of care. Only recently a provisional consensus definition has been suggested for agitation in cognitive disorders.[24] Beyond the behavioural phenotype, this new definition emphasizes the emotional distress and excess disability that is associated with agitation. Agitation may worsen during the evening hours, a phenomenon referred to as 'sundowning'.[25]

Delusions

Since delusions in dementia are found to sometimes correspond to reality or to be neither incorrigible nor held with absolute certainty, they may not represent psychotic symptoms in a narrow sense and should certainly not preclude the attempt to understand their meaning.[26]

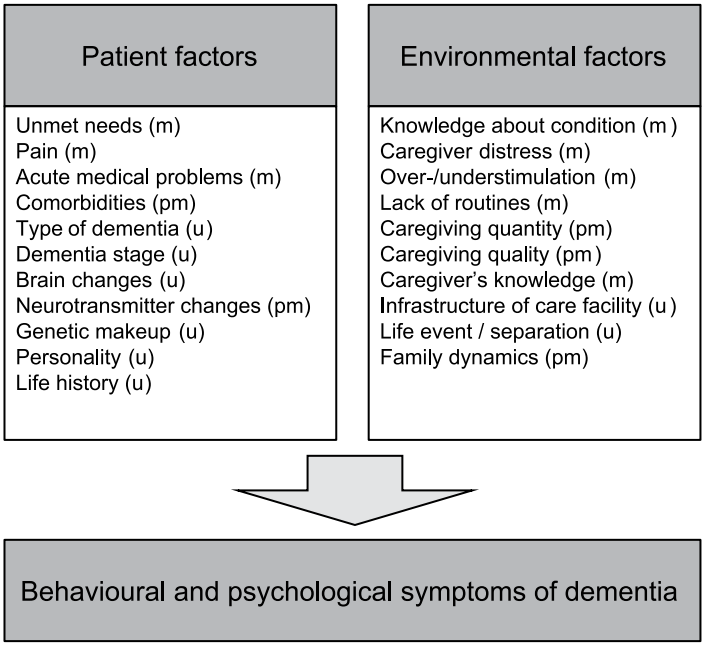

Figure 1. Simplified etiopathogenetic model of BPSD.
m, modifiable; pm, potentially modifiable; u, unmodifiable.

In terms of content, delusions in dementia are frequently persecutory in nature or revolve around theft – that is, lost objects,[27] danger, abandonment and the idea that one's house is not one's home.[26] Notably, only about half of the cases of delusions appear to lead to discomfort and are associated with behavioural disturbances.[28] A frequent subtype of delusions in dementia is the misidentification syndromes in which a patient consistently misidentifies persons, places, objects or events (e.g. Capgras syndrome).[29] Sensory impairment is widely considered a contributory factor in the development of certain delusions in dementia, most obviously in cases of Charles Bonnet syndrome in the context of visual impairment.

Apathy

Apathy is usually defined as loss of motivation and decreased interest in daily activities.[30] In the most severe forms, the affected patients may be unable to initiate almost any kind of directed activity, thus spending most of the day in bed or sitting in a chair. Apathy is one of the most frequent forms of BPSD and is associated with poor prognosis and increased mortality.[31,32] However, apathy rarely leads to hospital admissions since it is not usually as disruptive for caregivers as other BPSD.

Sleep problems and disturbances of circadian rhythms

Sleep problems are both risk factors and frequent symptoms of dementias and may also arise from comorbidities.[33,34] Sleep problems are a major contributor to caregiver burden. Even though the clinical need for effective treatments is high, the evidence base for treatments is limited.[35] In dementia with Lewy bodies (DLB), REM (rapid eye movement) sleep behaviour disorder (RBD) can be an early sign of the disease, with daytime fluctuations of attention, greater number of daytime naps and longer night sleeps.[36,37] RBD can also be seen in other synucleopathies such as Parkinson's disease and multiple system atrophy. In frontotemporal dementia (FTD), RBD is rare but may be confused with excessive nocturnal activity due to disturbed circadian rhythmicity.[38]

Etiopathogenesis of BPSD

More often than not the etiopathogenesis of BPSD is complex and multifactorial.[1] For the sake of didactic simplicity and practicability, the causative and contributing factors can be divided into biological, psychological and social or environmental factors (Figure 1).

Based on this perspective, a model for etiopathogenetic treatment of BPSD can be derived.

Biological perspective

Brain lesions and type of dementia. Dementia-related brain lesions and changes in neurotransmission have been linked to specific BPSD.[1] Their effect may be moderated by other biological factors such as comorbidity or treatment-related factors, as well as the individual's genetic make-up.

In the course of Alzheimer's disease (AD), psychotic symptoms were found to be associated with neuronal loss in several brain regions, including the hippocampus, parahippocampal gyrus and various brain stem nuclei.[39] In mixed (vascular and AD) dementia, vascular factors may trigger hallucinations, illusions, anxiety, dysphoria, aggression and delirium.[39–41]

Besides the aphasic forms, FTD is defined by behavioural features (bv-FTD or behavioural variant of FTD). These features are present from the early stages of the disorder and include loss of interest and apathy, as well as disinhibition, including inappropriate sexual behaviour and impulsive behaviours that are more frequent than in other dementias.[39] Both sporadic and familial forms of FTD have been described.[42,43] Similar to AD, a number of neurotransmitter and corticolimbic changes have been linked to behavioural disruptions in FTD.[1,42,44] Clearly, FTD is an important differential diagnosis, particularly in the early dementia stages. It is different from the frontal variant of AD,[45] and BPSD in FTD are probably less amenable to efficient treatment than in other forms of dementia.

Many neuroanatomical studies have been conducted that link BPSD to dementia-related brain lesions. For example, apathy was associated with hypoperfusion in the anterior cingulate cortex and fronto-subcortical structures,[1,46] giving rise to a disconnection model of apathy between the prefrontal cortex and the mediodorsal and anterior thalamic nuclei.[47] However, hypoperfusion in frontal or temporal lobes was also found to correlate with aggression and psychosis.[1] A variety of functional and structural parameters including, for example, white matter changes,[48] atrophy patterns and vascular damage contribute to BPSD.[48,49]

Changes in neurotransmission and neuromodulation. Changes in neurotransmission and neuromodulation have been found to correlate with BPSD. In AD, changes in cholinergic activity in the frontal and temporal cortices may be linked to aberrant motor activity and aggressive behaviour.[50,51] Visual hallucinations in DLB seem to be linked with cholinergic deficits in the temporal cortex.[50] In AD, aggression was reported to be related to reduced dopamine concentration in the temporal cortex.[44] Decreased norepinephrine neurons in the locus coeruleus are accompanied by aggressive behaviour.[1,52] Similarly, apathy was correlated with dopaminergic dysfunction in AD.[31,53,54] Serotonin concentration correlated positively with aggressiveness, depressed mood, anxiety, agitation and restlessness.[1] Interestingly, serotonin and, thus, SSRIs, may improve hippocampal neurogenesis,[55] and synaptic plasticity and survival of neurons are linked to the glutamatergic pathway.[1,56,57] Severe glutamate loss in AD may result in psychotic symptoms. Significant GABA decrease in the frontal and temporal cortex and high GABA plasma concentration were found in severe AD that correlated with depression and apathy.[1] As drugs acting on the above-mentioned neurotransmitter systems are legion, it is evident that many of them can either cause or favour the development of BPSD[58] or, on the contrary, have a potentially positive influence on them. Further pathway disorders related to neuromodulator and neuroendocrine systems have been proposed as correlates of BPSD, as well as circadian rhythms and sleep disorders,[1,59,60] including those of the hypothalamic–pituitary–adrenal axis or the homocystein metabolism.[61]

A number of findings suggest a genetic vulnerability for BPSD, though this field of research is still in its infancy. As an example, AD subjects who are *ApoEε4* carriers had more delusions and agitation/aggressive behaviours than non-*ApoEε4* carriers.[62] Given the implication in BPSD of neurotransmitter changes, it may come as no surprise that specific polymorphisms may predispose to BPSD.[62–64]

Physical disorders and pain. Physical disorders are often a central element in the understanding of BPSD and must be evaluated and treated accordingly.[1,6,58,65] Among the most frequent somatic causes of BPSD are pain, infections, electrolyte imbalances or metabolic disorders, urinary retention, constipation, cerumen and others. Any of these may cause BPSD and a thorough medical examination is therefore a requirement. Especially pain often leads to BPSD of various types, such as insomnia, aggressiveness or agitation.[66] Looking for pain-inducing factors and eliminating them is pivotal, as

pain is too often undetected and therefore undertreated in people with dementia.

Psychological and environmental perspective

Considering BPSD as the result of stressors combined with variable degrees of vulnerability, it is easy to imagine a host of psychological and systemic factors (personality, environmental elements both physical and emotional that contribute to the occurrence of BPSD).

Personality traits. Personality changes occur when dementia develops. In AD, a predictable change seems to occur independently of the previous personality, in that neuroticism usually increases while extraversion, openness and conscientiousness tend to decrease, with agreeability remaining more stable.[67] Furthermore and apart from its obvious face validity, there is increasing evidence that our personality – what we are as persons – contributes to the clinical expression of dementia. Thus, some personality traits may favour, or on the contrary protect against, BPSD. Thus, in AD, increased neuroticism as a premorbid personality trait may be associated with a higher risk for depression,[1,65,68,69] and even be a risk factor for cognitive decline and AD.[70,71] Patients who have been suspicious or aggressive before dementia starts are more likely to have BPSD than those without these traits.[1,69] However, such correlations have not always been found[68] and one of the more significant limitations of most of the studies currently available is the use of retrospective personality ratings, subjecting their findings to possible inaccuracies. Psychiatric diseases may be risk factors for dementia as this has been established for depression and for BPSD.[72]

Life events. Stressful life events in childhood or adulthood may favour BPSD in dementia through, among other etiopathogenic lines, increased vulnerability related to hippocampal hypotrophy and behavioural inhibition or insecure attachment.[56,73–75] Thus, overt attachment behaviour towards a family member or stranger was pronounced in old nursing home residents depending on the degree of cognitive impairment, suggesting that dementia eroded feelings of security and activated attachment behaviours.[76,77] Securely attached individuals with dementia displayed more positive affect than avoidantly attached individuals.[78]

Environmental risks. Environmental factors, both physical and social, are likely to precipitate or buffer BPSD. Thus, lower levels of BPSD are associated with well-being of nursing home residents, which is in turn related to environmental characteristics such as unobtrusive safety features, variety of spaces in environments with calm, single rooms available, small facility size, and optimization of levels of stimulation, taking into account the capacities of each patient.[1] Similarly, caregiver distress can exacerbate BPSD and family discord or altered communication in the family need to be assessed.[79,80]

Treatment

The treatment of BPSD is often highly challenging due to the complex etiopathogenesis of the symptoms and signs and the multi-morbidity of patients. BPSD management requires both a patient-centred and caregiver-centred focus and interventions to provide comfort to patients and alleviate caregiver burden are indispensable. Treating concomitant somatic diseases can reduce BPSD.[6] Effective pain management is part of a successful BPSD treatment.[81] Most expert recommendations and guidelines prefer non-pharmacological interventions as the first-line approach.[6,82,83] Although the evidence for most non-pharmacological strategies is weak, their efficacy is supported by long-standing clinical experience. Pharmacotherapy for BPSD is frequently provided, but it carries the risk of serious side-effects. Therefore, non-pharmacological therapies are considered the first choice and should also be continued when pharmacotherapy is necessary. In order to measure treatment effects, frequency and severity of BPSD should be quantified at baseline, possibly using a validated scale or questionnaire, such as the NPI[16] or BEHAVE-AD.[17,18] Moreover, several algorithms have been published to guide the diagnostic and therapeutic process for BPSD.[14] We suggest using the simplified BPSD-DATE algorithm (describe and measure, analyse, treat, evaluate; see Figure 2).

Non-pharmacological approaches

Due to the heterogeneous nature of non-pharmacological interventions, study designs vary widely in this area and call the generalizability of their results into question. Compared to pharmacological treatments of BPSD, the evidence base is much more limited. As of yet, it remains unclear

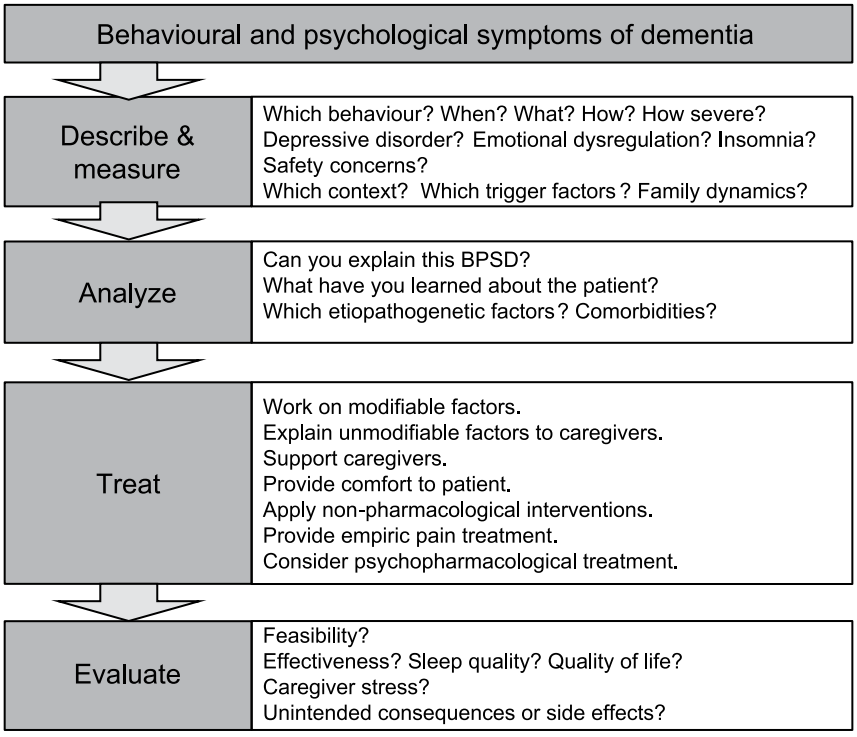

Figure 2. BPSD-DATE interventional algorithm.

whether or not heterogeneous non-pharmacological interventions are efficacious due to a common active but non-specific ingredient such as positive human interaction. At this point, the best scientific evidence exists for the use of home-based behavioural management techniques, caregiver-based interventions or staff training in communication skills, person-centred care, dementia care mapping against agitation[84,85] and music therapy against agitation and anxiety.[84]

Psychosocial interventions. Psychoeducation for patients and caregivers can reduce BPSD.[6,86–88] Multi-component single and group session programmes are effective if they focus on stressful events, provide both information about the disease and assistance, and allow for exchange on experiences as to how to deal with daily problems. Group sessions are more disburdening for caregivers when they include training in behavioural management techniques.[87,88] Coping strategy-based family carer therapy and tailored activities for people with dementia and their caregivers were found to improve quality of life of people with dementia living at home.[88] Psychoeducational interventions may be accompanied by social counselling, organizing assistance and supporting patients and caregivers. Psychosocial interventions, in general, decrease caregiver depression and can help delay the institutionalization of patients.[89]

Nursing care. The need-driven dementia-compromised behaviour model (NDB) can help understand BPSD as a dysfunctional expression of needs.[90] Based on this model, behavioural analysis in nursing care may recognize the patient's urgent needs and reveal their causes. Some factors causing BPSD, such as pain, hunger or thirst, can be satisfied immediately. However, personality characteristics and the biography of the patient, comorbidities and the lack of personal resources can complicate the course of the disease. The Serial Trial Intervention, based on the NDB model, uses systematic serial assessments and sequential trials of treatments to identify and treat unmet needs that may be the underlying cause of BPSD. It has been shown to reduce BPSD and the use of psychotropic drugs.[91] Special nursing care interventions targeting vocalization[92] and sexual disinhibition[93] may be helpful to comfort patients.

Physical activity. Regular exercise improves physical fitness, behaviour, cognition and functioning in older people.[94] There is strong evidence that regular physical activity improves physical,

cognitive, functional and behavioural outcomes also in patients with dementia and can help reduce BPSD.[94] Usually, training programmes are based on walking (mobility training) or they combine walking with different types of isotonic exercises.

Sensory stimulation and music therapy. Music therapy and multisensorial stimulation techniques such as snoezelen are effective in reducing agitation and disruptive behaviour during sessions and immediately after the intervention.[6,86] However, there is no evidence for long-term effects. Biography-related music and combination with sensory stimulation seem to be more effective.

Reality orientation and cognitive stimulation therapy. These interventions are based on the idea that a better orientation in daily life to persons, time or surroundings can improve BPSD.[86] Reality orientation therapy is more effective in combination with other techniques in improving mood and decreasing BPSD. Derived from reality orientation therapy, cognitive stimulation therapy addresses current problems in functioning using information processing.[86] There are some immediate effects on BPSD, but the data are inconsistent.

Validation therapy. This patient-centred technique intends to resolve unfinished conflicts by encouraging and positively validating expression of feelings.[86] There is some evidence that positively validating expression of feelings may reduce irritability.

Reminiscence therapy. Reminiscence therapy uses objects from daily life to stimulate memory and enable people to value their experiences.[86] This intervention can improve mood.

Psychotherapeutic interventions. Psychological therapies have been investigated in mild to moderate dementia. The highest level of evidence of efficacy is available for cognitive behavioural techniques.[6,86,95,96] Focusing on daily problems, psychotherapeutic interventions are more effective if caregivers are involved in the process. Combination with psychoeducation and family counselling improves effectiveness.[96,97] Behavioural management techniques improve depression, anxiety, aggression and agitation in dementia.[86] The effect is significant and lasts for months. Since caregivers can also develop depression during the care process, they can also benefit from individual psychotherapy.

Psychopharmacotherapy

Since patients with dementia are particularly vulnerable to adverse effects of drugs, the indication for psychopharmacotherapy in BPSD has to be discussed very critically. Multi-morbidity and polypharmacy are interacting factors complicating the use of pharmacotherapy. Most drugs are not approved for BPSD and their use is therefore off-label. A detailed clinical and laboratory examination including history of medication and an electrocardiogram should precede psychopharmacotherapy. Psychotropic medication use should be limited in time and stopped after a gradual reduction when BPSD improve. Drug metabolism is altered in elderly patients and compared to younger patients they usually need lower doses of psychotropic drugs.

Antidementia drugs. There is some evidence that cholinesterase inhibitors and memantine may be useful in the management of BPSD.[6,14,98–101] Cholinesterase inhibitors may improve affective features in mild to moderate dementia. Cholinesterase inhibitors and memantine may be effective to treat BPSD. Indeed, donepezil may alleviate the following BPSD in mild to moderate dementia: apathy, depression, tension, irritability. There are similar findings for galantamine and rivastigmine. However, treatment of agitation in AD by donepezil appears to be inefficient. In conclusion, cholinesterase inhibitors have a certain efficacy on negative symptoms.[6,102] Memantine may be more effective on positive symptoms including agitation, delusions and hallucinations, as well as aggression in moderate to severe AD.[6,102] However, more recent trials specifically designed for treatment of agitation challenge these findings as they failed to demonstrate a benefit.[99,103,104] Finally, antidementia drugs may reduce the incidence of BPSD. There are also data that provide some evidence for the preventive efficacy of *Ginkgo biloba* extract EGb 761® in the treatment of dementia patients with clinically relevant BPSD.[105]

Antidepressants. Depression and anxiety are among the most common BPSD and an effective antidepressive therapy in dementia can improve both cognition and affective symptoms as well as other forms of BPSD, such as agitation and aggressiveness.[6,14,106] Tricyclic antidepressants are not recommended because of their anticholinergic adverse events. SSRIs have reasonable tolerability and favourable treatment response. In dementia, SSRIs (specifically citalopram) are as efficacious as atypical antipsychotics for treating

agitation.[107] SSRIs can be associated with severe adverse effects such as QT-prolongation and hyponatraemia.

Antipsychotics. First, it is important to state that antipsychotics have not been approved for clinical use in dementia, except for risperidone, at least in some countries. Thus, clinicians ought to refer to their country's legislation before introducing an antipsychotic drug to treat BPSD. Atypical antipsychotics such as risperidone and aripiprazole are among the most often (and probably too often) prescribed drugs in BPSD. They are effective in the treatment of psychotic symptoms, agitation and aggression.[2,14,108,109] Haloperidol may be considered in the treatment of delirium in dementia, but it is not recommended for a different use in dementia. Haloperidol is only recommended for delirium because of its high potential for side-effects. Adverse events associated with atypical antipsychotics include anticholinergic effects, orthostatic hypotension, seizures, metabolic syndrome, weight gain, extrapyramidal symptoms, sedation and QT-prolongation. The increased mortality and the risk for cerebrovascular incidents have led to a black box warning for the use of antipsychotics in dementia. Antipsychotics can be necessary and helpful in the treatment of certain BPSD, but their use must be limited in time. Regular evaluations of risks and benefits are necessary throughout the course of the treatment.[110] While the evidence on the efficacy of quetiapine for BPSD is mixed, it is widely used clinically.[111] Due to its favourable side-effect profile, particularly regarding extrapyramidal signs, quetiapine may be of particular value for BPSD, especially in patients with Parkinsonian features, despite conflicting evidence.[112]

Mood stabilizers. Although carbamazepine shows some benefit for agitation in dementia, mood stabilizers are often associated with severe side-effects.[2,14,113] Thus, valproic acid is not recommended. There is some clinical experience and limited evidence for gabapentine and lamotrigine in the treatment of BPSD.

Benzodiazepines. Evidence for the efficacy of benzodiazepines in BPSD is lacking. Benzodiazepines are associated with sedation, dizziness, falls, worsening cognition, respiratory depression, dependency and paradoxical disinhibition in the elderly. They are thus only recommended for the management of an acute crisis,[6,14] if other methods fail. Their use must be limited in time and they should not be prescribed as hypnotics.

Other substances. Hypnotics such as zopiclone, zolpidem or zaleplone can have similar side-effects as benzodiazepines.[6] They are used for sleep disorders in dementia over a limited period of time and at small doses. Sedative antidepressants such as trazodone seem to improve sleep duration. Melatonin and melatonin receptor agonists can be effective in treating circadian sleep disorders.[34,35]

Biological therapies

Light therapy (in the morning) and light therapy in combination with melatonin (at bedtime) may be useful to treat sleep or circadian rhythm disorders, 'sundowning' and day sleepiness,[114] but sleep deprivation is not recommended in BPSD.[6] Indeed, there is a higher risk of agitation and other BPSD may appear due to insomnia.[65]

Electroconvulsive therapy may be helpful in individual situations. Similarly, repeated transcranial magnetic stimulation may become a useful method, but the study of this method to treat BPSD is still in its infancy.

Conclusion

BPSD occur on an almost regular basis as dementia evolves, regardless of the dementia type. BPSD are a heterogeneous group of symptoms and signs, but all of them may cause significant suffering in patients and caregivers. The causes of and risk factors for BPSD are multiple, even in a single patient, with interacting biological, psychological and social/environmental causes and vulnerability factors. Taking a detailed history and performing a sound clinical investigation including the patient and their family or care team are essential. In order to arrive at an individualized treatment plan, a therapeutic decision tree should be established taking into account the patient's individual and their environmental risk profile. Psychosocial treatments are pivotal. Often, combining different non-pharmacological approaches precedes drug treatment that can be added if required. Consequently, an interventional algorithm is proposed to take care of patients suffering BPSD (Figure 2). Regular assessments of the treatment plan and any prescriptions must be carried out to detect signs of relapse and to stop any drug that has become inappropriate. Even with optimal management, BPSD will not disappear completely in some cases and will remain challenging for all involved parties.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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